

On the noise modelling in a nerve fiber

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Abstract

We present a novel mathematical approach to model noise in dynamical systems. We do so by considering dynamics of a chain of diffusively coupled Nagumo cells affected by noise. We show that the noise in transmembrane current can be effectively modelled as fluctuations in electric characteristics of the membrane. The proposed approach to model noise in a nerve fibre is different from the standard additive stochastic current perturbation (the Langevin type equations).

Keywords: Nagumo equation, noise, dynamic sampling

1. Introduction

A typical nerve fiber is coated in myelin (the myelin sheath consists of a single Schwann cell which is wrapped about 100 around the nerve fiber) with spatially periodic gaps, the nodes of Ranvier. Roughly the myelin sheath increases the membrane resistance by a factor of about 100 and decreases the membrane capacitance by a factor of about 100. Typically, the width of the node of Ranvier is about $1\mu\text{m}$, the distance between nodes (the length of myelin sheath) is about 1.5mm that is close to $100d$, where d is the nerve fiber diameter. Transmembrane ion flow occurs only at the nodes of Ranvier. Diffusive coupling corresponds to axial currents between nodes and allows propagation of changes in the transmembrane potential (action potential) in the spatial variable. Nerve fibers behave as intrinsic spatially discrete systems. The biological reason for such discrete structure: propagation of action potential along myelinated fibre is faster compare to that in nonmyelinated because of its saltatory propagation between nodes (speed in a myelinated fibre is around 100 m/s and in a nonmyelinated fiber is $1 \div 5\text{ m/s}$). For further details of the model, physical parameters and equivalent electric circuit we refer to [1].

The idea that noise can play a positive role and benefit neural function is relatively new. Just 60 years ago it was commonly accepted that the noise is destructive to neural encoding [2, 3]. Today it is well established that noise plays constructive role in the nerve system [4–8]. This new paradigm was initiated by research on stochastic resonance phenomena. It was shown that the stochastic resonance improves the transfer of information [9, 10].

In this Letter, we accomplish two goals. First, we propose and study the deterministic scheme for modelling of noise in a nerve fiber. This scheme involves dynamical fluctuations of electric characteristics of the membrane together with their negative feedback control depending on the noise intensity. Then, to ensure ergodicity property of the dynamics, we combine this dynamical feedback control with a stochastic perturbation. In contrast to the random noise model (see Section 2) our scheme operates with the only white noise process that indirectly affect initial dynamics. While we do not claim that our scheme to model noise in a nerve fibre is better than standard additive stochastic current perturbation (the Langevin type equations), we state our approach as different.

We consider a lattice of diffusively coupled Nagumo cells described, in absence of noise, by the equations, $\dot{u}_i = \Delta u_i + f(u_i)$, $i \in \mathbb{Z}$ is a spacial index, where $f(u) : \mathbb{R} \rightarrow \mathbb{R}$ has a bistable character, for example $f(u) =$

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$-ku(u - \alpha)(u - 1)$, $0 < \alpha < 1$, $k > 0$; $\Delta u_i \equiv u_{i+1} - 2u_i + u_{i-1}$ is the standard 3 point discretization of the Laplacian (discrete Laplacian), and $l > 0$ is a coefficient of the diffusive coupling. In addition we define “potential” $V(u)$ by the differential equation, $V'(u) = -f(u)$, $V(0) = 0$. In these equations variable u corresponds to a transmembrane electric potential, k corresponds to the membrane conductance, α is the threshold potential. Besides modelling of the action potential propagation along a nerve fibre, this lattice system is important in another different areas of research [11–13].

In cases where $i \in I \subset \mathbb{Z}$ and I is bounded, we consider this set with respect to boundary conditions, for example of the Neumann type. For what follows, it is convenient to represent Nagumo equations in the variational form. Define the “energy” functional, $\mathcal{V}[u] = \sum_{\{i\}} [\frac{1}{2}l(\nabla u_i)^2 + V(u_i)]$, where $\nabla u_i = u_i - u_{i-1}$ is the discrete gradient. Hereafter we accept short notations: $\frac{\partial}{\partial u_i} \equiv \partial_i$, $\frac{\partial^2}{\partial u_i^2} \equiv \partial_i^2$, $\frac{\partial}{\partial t} \equiv \partial_t$, and so on. With these definitions, rewrite the lattice of the diffusively coupled Nagumo equations in the gradient form,

$$\dot{u}_i = -\partial_i \mathcal{V}[u], \quad i \in \mathbb{Z}. \quad (1)$$

It is easy to reveal that $\mathcal{V}[u]$ is the Lyapunov functional since $\dot{\mathcal{V}}[u] = -\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 \leq 0$. Steady states of equations (1) are the extrema of functional $\mathcal{V}[u]$. The minima and maxima of $\mathcal{V}[u]$ correspond respectively to stable and unstable solutions of equation (1). Suppose $\mathcal{V}[u] > -\infty$ and define for a continuous function $A(u)$ the time averaging, $\overline{A(u)} = \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T A(u(t)) dt$. Applying the time averaging to $\dot{\mathcal{V}}[u] = -\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2$ ($\mathcal{V}[u] > -\infty$) we arrive at the equation, $\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 = 0$. Thus the system spends almost all time at states of extrema of $\mathcal{V}[u]$. These extrema are solutions of the discrete lattice equation, $l\Delta u_i - \partial_i \mathcal{V}[u] = 0$, $i \in \mathbb{Z}$. This equation is implied to be equipped with some boundary conditions. For our purpose we accept the following conditions, $\nabla u_i \rightarrow 0$ as $i \rightarrow \pm\infty$.

2. Random noise

To model the influence of noise on deterministic system (1), it is widely accepted in the literature that the noise is implemented in (1) by the additive stochastic currents, $\xi_i(t)$, $i \in \mathbb{Z}$, where $\{\xi_i(t)\}_{i \in \mathbb{Z}}$ is the set of independent standard generalized Gaussian δ -correlated processes completely characterized by the first two cumulants, $\langle \xi_i(t) \rangle = 0$ and $\langle \xi_i(t) \xi_j(t') \rangle = \delta_{ij} \delta(t - t')$; $\langle \dots \rangle$ means averaging over all realizations of the random perturbations. The set of stochastic differential equations corresponding to (1) takes the form, $\dot{u}_i = l\Delta u_i + f(u_i) + \sqrt{2D}\xi_i(t) = -\partial_i \mathcal{V}[u] + \sqrt{2D}\xi_i(t)$, $i \in \mathbb{Z}$, where D is the noise intensity (we suppose that noise does not depend on node). It is convenient for what follows to represent this set as

$$\dot{u}_i = -\lambda \partial_i \mathcal{V}[u] + \sqrt{2\lambda D} \xi_i(t), \quad i \in \mathbb{Z}, \quad (2)$$

where a reference time scale λ is explicitly introduced. Rescaling time in (2), $t \rightarrow \lambda^{-1}t$, and taking into account scaling property of the white noise, we arrive at the case $\lambda = 1$.

In system (2) dissipative processes and random perturbations equilibrate one another. In respect of the “energy”, $\mathcal{V}[u]$, we arrive at the stochastic differential equation (we specify this equation in the sense of Stratonovich (e.g. [14])),

$$\dot{\mathcal{V}}[u] = -\lambda \sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 + \sqrt{2D\lambda} \sum_{\{i\}} \partial_i \mathcal{V}[u] \xi_i(t). \quad (3)$$

Equation (3) demonstrates in what way the noise affects the “energy” and defines rate of its (stochastic) fluctuations. Assume that $\mathcal{V}[u] > -\infty$. Then after averaging over all realization of the random perturbations we arrive at the relation, $-\langle \sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 \rangle + D \langle \sum_{\{i\}} \partial_i^2 \mathcal{V}[u] \rangle = 0$, that does not depend on λ ; we assume $\langle V[u] \rangle = \text{const}$. The relation can be derived either by an elementary calculation or elegantly applying Novikov’s formula [15]. This is an important relation that connects the noise intensity to configurational ensemble averages and thus can be considered as the definition of the noise intensity. In what follows we conjecture that the analogue formula involving the time averaging instead of the ensemble averaging, $-\overline{\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2} + D \overline{\sum_{\{i\}} \partial_i^2 \mathcal{V}[u]} = 0$, is valid and thus defines the noise intensity in the framework of deterministic dynamics. In order to deepen the conjecture and to describe dynamics of the deterministic fluctuations, we have to further presume the rate of dynamic fluctuations (r.d.f.) in the form,

$$\text{r.d.f.} \sim -\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 + D \sum_{\{i\}} \partial_i^2 \mathcal{V}[u], \quad (4)$$

that is instead of random perturbations (that do not present in deterministic dynamics) we need to consider dynamic fluctuations of an appropriate variable. Indeed, in absence of random perturbations we have to adopt another way to properly perturb the system. Fluctuations in the electric characteristics of membrane are conjugate to that in electric current across the membrane. Thus it is reasonable to consider a certain electric characteristic of the membrane, supposedly RC (where R is resistance and C is capacitance), that defines a time scale and allows this characteristic to dynamically fluctuate.

With random noise its intensity D is commonly considered as an independent parameter. Indeed, the Fokker-Planck operator corresponding to (2) has the form, $\mathcal{F}^*\rho \equiv -\sum_{(i)} \partial_i (\partial_i \mathcal{V}[u]\rho) + D \sum_{(i)} \partial_i^2 \rho$. The Fokker-Planck equation associated with \mathcal{F}^* , $\partial_t \rho = \mathcal{F}^* \rho$, allows the invariant solution, $\rho_\infty[u] \sim \exp\{-D^{-1}\mathcal{V}[u]\}$. We prove the identity, $\mathcal{F}^* \rho_\infty[u] \equiv 0$, by straightforward calculation. It is known that this distribution and the corresponding probabilistic measure, $d\mu \sim \exp\{-D^{-1}\mathcal{V}[u]\} \prod_{(i)} du_i$, are typically unique for dynamics (2). In a word, stochastic dynamics (2) is typically ergodic. This means that for every continuous function A , $\int A(u) d\mu = \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T A(u(t)) dt$, almost for sure for all initial values $u(0)$. The invariant measure relates to infinite time interval. Thus scaling the time variable does not affect the measure. The invariant (equilibrium) distribution ρ_∞ demonstrates explicit dependence on the noise intensity, D . The only constraint on D arise when we presume a nondestructive role of the noise. Namely, in the case of a cubic nonlinearity of $f(u)$, the general form of $V(u)$ is double-well. Then the noise can induce transition from one well to another, it depends on D , and is expected to be a slow process.

Now we can pose the problem: Given a probability measure $d\mu$ (or an augmented measure on an extended phase space). It is necessary to find a dynamics such that $\lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T A(u(t)) dt = \int A(u) d\mu$ for every continuous function A . We say this is dynamic modelling of the noise and assume $d\mu \sim \exp\{-D^{-1}\mathcal{V}[u]\} \prod_{(i)} du_i$ as the invariant (ergodic) measure for this dynamics.

3. Deterministic modelling of noise

Now we will put together the above observations, - that the rate of feedback control of dynamic fluctuations and the invariant measure, depend on the noise intensity, - to derive a model of a deterministic noise of intensity D in a nerve fibre. The requirements are:

- Dynamics of u depends on the external dynamic variables (e.g., λ is endowed with its own equation of motion);
- Rate of deterministic dynamic fluctuations is directly related to (4) (e.g., the rate of fluctuations is a measure of the influence of environment on electrical characteristics of the membrane);
- Measure $d\mu \sim \exp\{-D^{-1}\mathcal{V}[u]\} \prod_{(i)} du_i$ is invariant for the dynamics;
- Dynamics is ergodic.

In other words, we will sample the invariant measure, $d\mu \sim \exp\{-D^{-1}\mathcal{V}[u]\} \prod_{(i)} du_i$, by the method proposed in [16, 17] and to incorporate the noise intensity, D , into dynamics in accordance with (4). This procedure is just reasonable since involves dynamical fluctuations of the membrane electrical characteristics. To correctly sample the invariant measure, dynamics must be ergodic.

Consider dynamics in the extended phase space $(\{u_i\}, \lambda, \{\eta_i\})$,

$$\dot{u}_i = -\lambda \partial_i \mathcal{V}[u] + \eta_i, \quad \dot{\lambda} = g(u), \quad \dot{\eta}_i = h_i(u), \quad i \in \mathbb{Z}; \quad (5)$$

functions $g(u)$ and $h_i(u)$ are to be determined. The extra dynamical variables λ and η_i model the environment and thus they represent the noise effect on the Nagumo dynamics.

Remark. Term η_i in the dynamical equations (5) is important. Indeed, assume $\eta_i \equiv 0$. Then, at an equilibrium $\partial_i \mathcal{V}[u] = 0$, the evolution comes to halt and no longer fluctuates, irrespective of the time dependence of λ . For initial conditions with $\partial_i \mathcal{V}[u] \neq 0$ after a time variable rescaling, it is a gradient flow as defined in [18], and all phase space trajectories moves along paths with equilibrium points at either end. Thus dynamics is not ergodic. For a further discussion we refer to [16, 17].

To determine functions $g(u)$ and $h_i(u)$, calculate, on the analogy of (3),

$$\mathcal{V}[u] = -\lambda \sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 + \sum_{\langle ij \rangle} \eta_{ij} \partial_i \mathcal{V}[u]. \quad (6)$$

Respect to the second term on r.h.s. of (6) we put the following requirement to the time average, $\overline{\sum_{\langle ij \rangle} \eta_{ij} \partial_i \mathcal{V}[u]} = 0$. A series of η -dynamics satisfies this condition. Two principal limit cases are: fluctuations of current in different nodes are independent or synchronous. Correspondingly we endow variables $\{\eta_{ij}\}$ with the following dynamical equations,

$$\dot{\eta}_{ij} \sim \partial_i \mathcal{V}[u], \quad i \in \mathbb{Z}, \quad \text{and} \quad \dot{\eta}_{ij} \sim \sum_{\langle jk \rangle} \partial_j \mathcal{V}[u], \quad \forall i \in \mathbb{Z}. \quad (7)$$

However, respect to the first term in r.h.s. of (6), we cannot repeat the trick and set $\dot{\lambda} \sim \sum_{\{i\}} (\partial_i \mathcal{V}[u])^2$, since this results in no noise effect. To overcome this difficulty, we implement conjecture (4) into λ -dynamics and (6), and explicitly set

$$\dot{\lambda} \sim \sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 - D \sum_{\{i\}} \partial_i^2 \mathcal{V}[u]. \quad (8)$$

Lemma 1. Assume λ to be bounded variable, its dynamics is given by (8) and $\overline{\sum_{\langle ij \rangle} \eta_{ij} \partial_i \mathcal{V}[u]} = 0$ (e.g. one of dynamical equations (7)). Then $\overline{\lambda \sum_{\{i\}} \partial_i^2 \mathcal{V}[u]} = 0$.

Proof. First we multiply (8) by λ and take into account equation (6). Then we apply the time averaging to the resulted equation. Thus we easily accomplish lemma. Indeed,

$$0 = -\lambda \left[\sum_{\{i\}} (\partial_i \mathcal{V}[u])^2 - D \sum_{\{i\}} \partial_i^2 \mathcal{V}[u] \right] = -\overline{\dot{\mathcal{V}}[u]} + \overline{\sum_{\langle ij \rangle} \eta_{ij} \partial_i \mathcal{V}[u]} - D\lambda \sum_{\{i\}} \partial_i^2 \mathcal{V}[u] = D\lambda \sum_{\{i\}} \partial_i^2 \mathcal{V}[u].$$

□

This lemma together with the equations (6)-(8) allows us to determine functions $g(u)$ and $h_i(u)$ explicitly,

$$g = \frac{1}{Q_\lambda} \sum_{\{i\}} [(\partial_i \mathcal{V}[u])^2 - D \partial_i^2 \mathcal{V}[u]], \quad h_i = -\frac{1}{Q_\eta} \partial_i \mathcal{V}[u] \text{ or } h_i = -\frac{1}{Q_\eta} \sum_{\langle ij \rangle} \partial_j \mathcal{V}[u], \quad i \in \mathbb{Z}, \quad (9)$$

where Q_λ and Q_η are parameters. Variables η_{ij} and corresponding functions h_i and not unique and dynamical equations can be simplified.

To verify the requirement on the invariant measure we prove the theorem.

Theorem 2. Assume the extended dynamics in form (5) where functions g and h_i are given by (9), $Q_\lambda > 0$ and $Q_\eta > 0$. Then the augmented measure,

$$d\mu \sim \exp\{-D^{-1} \mathcal{V}[u]\} \exp\left\{-D^{-1} \left(\frac{1}{2} Q_\lambda \lambda^2 + \frac{1}{2} Q_\eta \sum_{\langle ij \rangle} \eta_{ij}^2\right)\right\} \prod_{\langle ij \rangle} du_i d\lambda d\eta_{ij} = \rho_\infty \prod_{\langle ij \rangle} du_i d\lambda d\eta_{ij}, \quad (10)$$

is invariant for the extended dynamics.

Remark. It should be noted that the η -dynamics is not unique and so correspondingly it allows a variety of η -factors of the augmented measure, although they are still Gaussian. E.g., with the synchronous dynamical fluctuations, $\dot{\eta} = -\frac{1}{Q_\eta} \sum_{\langle ij \rangle} \partial_j \mathcal{V}[u]$, we arrive at $\exp\{-D^{-1} \frac{1}{2} Q_\eta \eta^2\} d\eta$. However all cases can be treated analogously.

Proof. The Liouville operator corresponding to the dynamics in the extended phase space (5) has the form, $\mathcal{L}^* \rho = -\sum_{\langle ij \rangle} \partial_i [(-\lambda \partial_i \mathcal{V}[u] + \eta_{ij}) \rho] - \partial_\lambda [g(u) \rho] - \sum_{\langle ij \rangle} \partial_{\eta_{ij}} [h_i(u) \rho]$, and the Liouville equation reads $\partial_t \rho = \mathcal{L}^* \rho$. Therefore, to prove the theorem we have to prove the identity, $\mathcal{L}^* \rho_\infty \equiv 0$, that means the dynamics (5) preserves the augmented measure (10). A straightforward calculation of all partial derivatives that are involved in $\mathcal{L}^* \rho_\infty$ with further simplification brings to the required identity, $\mathcal{L}^* \rho_\infty \equiv 0$. The theorem is proved. □

From the perspective of numerical simulations and further mathematical analysis, *e.g.* the Hamiltonian representation of the proposed dynamics, it is important to find a first integral of motion. We accomplish this task with the following lemma.

Lemma 3. *Let the dynamical system (5) and (9) be augmented with the redundant dynamical variable ζ , $\dot{\zeta} = -\lambda \sum_{(i)} \partial_i^2 \mathcal{V}[u]$. Then $I = \mathcal{V}[u] + \frac{1}{2} Q_\lambda \lambda^2 + \frac{1}{2} Q_\eta \sum_{(i)} \eta_i^2 - D\zeta$ is the first integral of the augmented dynamical system.*

Proof. We derive $\dot{I} = 0$ by direct calculation. \square

Remark. Since the origin of coordinates of the redundant variable ζ is arbitrary, it is always possible for an arbitrary fixed trajectory to set $I = 0$. I is apparent control parameter in numerical simulations. Besides, I is related to ρ_∞ and thus can be considered from a perspective of the Hamiltonian reformulation of dynamics on the level set $I = 0$ [16]. However we do not consider this problem here.

We can now ask whether the dynamics (5),(9) is ergodic. There is no a definite answer to this question. Following [16] we can apply the Frobenius theorem of differential geometry [19] but this provides with a partial answer only. Here, in order to provide ergodicity, we adopt the method proposed in [16] and rigorously investigated in [20]. Namely, we add a Gaussian random noise to the λ -dynamics. In contrast to the model outlined in Section 2, where stochastic currents are added at each node, this approach relies on single and indirect stochastic perturbation. Experiments [20] reveal that, in context of the molecular dynamics, it results in a relatively weak perturbation effect on deterministic dynamics. Thus, we reformulate λ -dynamics (5) in the form,

$$\dot{u}_i = -\lambda \partial_i \mathcal{V}[u] + \eta_i, \quad \dot{\lambda} = g(u) - \gamma \lambda + \sqrt{2\gamma D Q_\lambda^{-1}} \xi(t), \quad \dot{\eta}_i = h_i(u), \quad i \in \mathbb{Z}, \quad (11)$$

where $\gamma > 0$ is a parameter.

Theorem 4. *Assume stochastically perturbed extended dynamics in the form (11) where functions g and h are given by (9), $Q_\lambda > 0$, $Q_\eta > 0$. Then the augmented measure (10) is invariant for this dynamics.*

Proof. The Fokker-Planck operator corresponding to (11) has the form, $\mathcal{F}^* \rho = \mathcal{L}^* \rho + \gamma \partial_\lambda [(\lambda + D Q_\lambda^{-1} \partial_\lambda) \rho]$, and the Fokker-Planck equation reads $\partial_t \rho = \mathcal{F}^* \rho$. After a series of routine calculations we arrive at $\mathcal{F}^* \rho_\infty \equiv 0$. Thus the stochastically perturbed dynamics (11) preserves the augmented measure (10). \square

Test simulations. Single cell dynamics.

Low dimensional systems often reveal the ergodicity problem in a probability distribution dynamical sampling. For this reason, it is important to test the presented noise modelling method capable of generating the right statistic for a single Nagumo cell. We choose for this purpose $f(u) = -4u(u - \alpha)(u - 1)$. Simulations are performed using global parameters $D = 0.04$ and $\gamma = 1$, for $t = 10^6$. Figure 1 shows the probability distribution of the u variable calculated

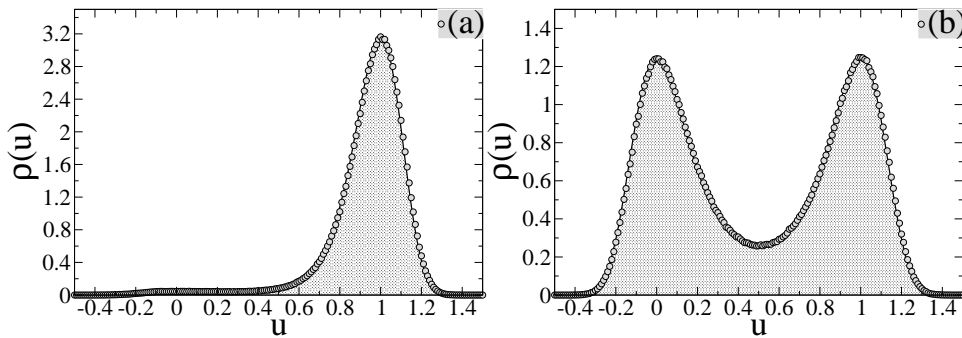


Figure 1: Probability distributions of u variable (shown on background of exact analytical distribution). Densities are calculated as normalized sojourn distributions. Correspondingly, (a) $\alpha = 0.25$ and (b) $\alpha = 0.5$.

with the dynamical equations and compared with exact analytical distribution. Their solid agreement brings a severe test of our approach.

4. Conclusion

We have presented a novel mathematical approach to model noise in dynamical systems. We do so by considering dynamics of a chain of diffusively coupled Nagumo cells affected by noise. We have shown that the noise in transmembrane current can be effectively modelled as fluctuations in electric characteristics of the membrane. Test simulations give a solid support to the mathematical scheme. The proposed approach to model noise in a nerve fibre is different from the standard additive stochastic current perturbation and thus demonstrates a potential for further application.

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References

References

- [1] J. Keener, J. Sneyd, *Mathematical Physiology*, 2nd Edition, Vol. 1. Cellular Physiology, Springer, 2009.
- [2] P. Fatt, B. Katz, Some Observations on Biological Noise, *Nature* 166 (1950) 597–598.
- [3] P. Fatt, B. Katz, Spontaneous subthreshold activity at motor nerve endings, *J Physiol.* 117 (1952) 109–128.
- [4] R. S. Zucker, Can a synaptic signal arise from noise?, *Neuron* 38 (6) (2003) 845–846.
- [5] G. Sharma, S. Vijayaraghavan, Modulation of presynaptic store calcium induces release of glutamate and postsynaptic firing, *Neuron* 38 (6) (2003) 929–939.
- [6] J. G. Milton, Noise as therapy: a prelude to computationally-based neurology?, *Ann Neurol* 58 (2005) 173–174.
- [7] A. A. Faisal, L. P. J. Selen, D. M. Wolpert, Noise in the nervous system, *Nature Reviews Neuroscience* 9 (2008) 292–303.
- [8] G. Deco, E. T. Rolls, R. Romo, Stochastic dynamics as a principle of brain function., *Prog Neurobiol* 88 (2009) 1–16.
- [9] L. Gammaitoni, P. Hänggi, P. Jung, F. Marchesoni, Stochastic resonance, *Rev. Mod. Phys.* 70 (1) (1998) 223–287.
- [10] A. Samoletov, M. Chaplain, V. Levi, Global spatiotemporal order and induced stochastic resonance due to a locally applied signal., *Phys Rev E* 69 (2004) 045102.
- [11] J. Cahn, Theory of crystal growth and interface motion in crystalline materials, *Acta Metallurgica* 8 (8) (1960) 554–562.
- [12] T. Erneux, G. Nicolis, Propagating waves in discrete bistable reaction-diffusion systems, *Physica D: Nonlinear Phenomena* 67 (1-3) (1993) 237–244.
- [13] P. Bates, A. Chmaj, A Discrete Convolution Model for Phase Transitions, *Archive for Rational Mechanics and Analysis* 150 (4) (1999) 281–368.
- [14] B. Øksendal, *Stochastic differential equations: an introduction with applications*, Springer Verlag, 2003.
- [15] V. Klyatskin, A. Vinogradov, *Dynamics of stochastic systems*, Elsevier, 2005.
- [16] A. Samoletov, C. Dettmann, M. Chaplain, Thermostats for "slow" configurational modes, *J. Stat. Phys.* 128 (2007) 1321–1336.
- [17] A. A. Samoletov, C. P. Dettmann, M. A. J. Chaplain, Notes on configurational thermostat schemes., *J Chem Phys* 132 (24) (2010) 246101.
- [18] A. Katok, B. Hasselblatt, *Introduction to the modern theory of dynamical systems*, Cambridge Univ Press, Cambridge, 1996.
- [19] S. Lang, *Introduction to differentiable manifolds*, Springer Verlag, 2002.
- [20] B. Leimkuhler, E. Noorizadeh, F. Theil, A gentle stochastic thermostat for molecular dynamics, *Journal of Statistical Physics* 135 (2009) 261–277.